Preventing the sexual transmission of HIV:

Lessons learned and opportunities for the future

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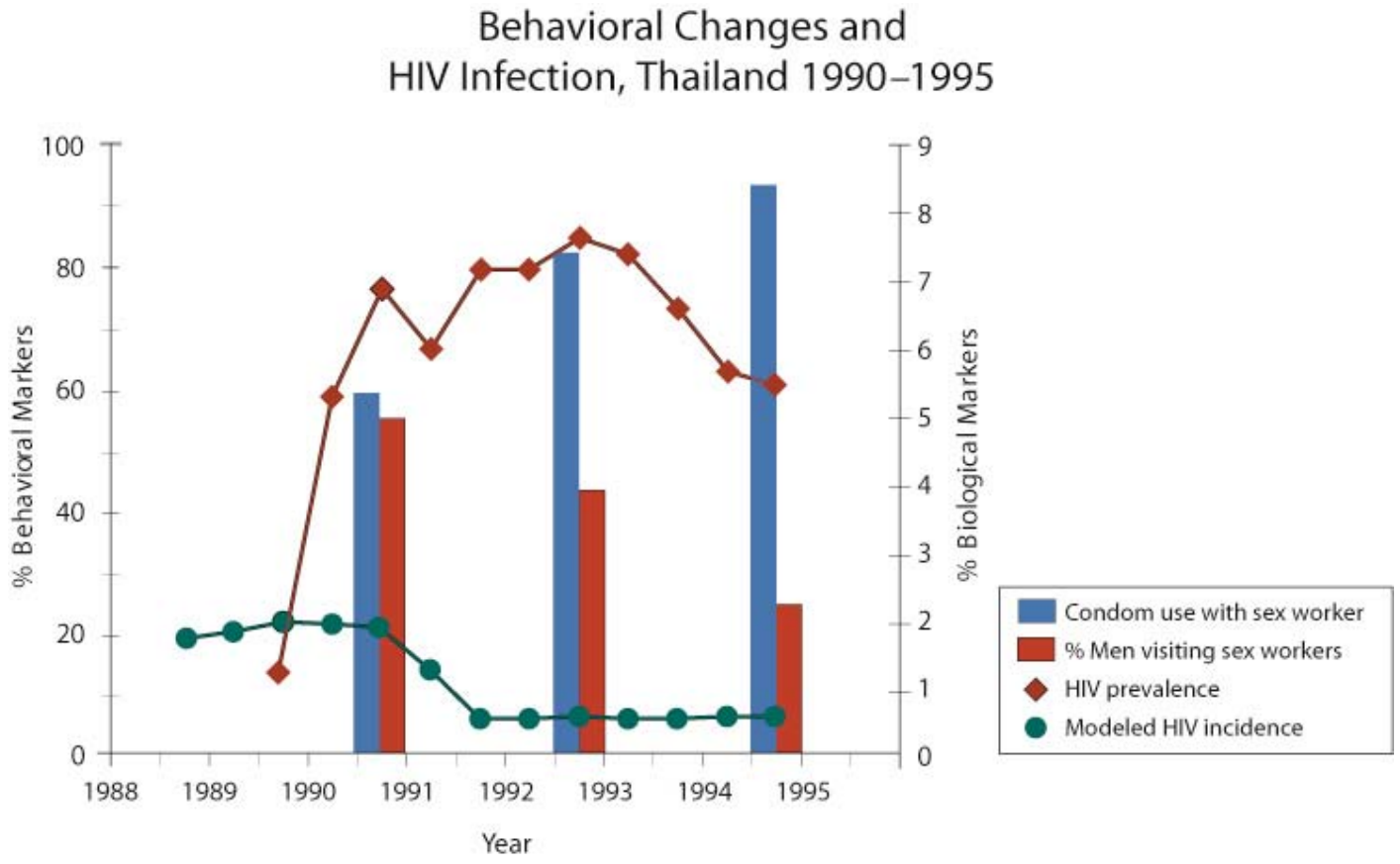
August 2005

Brief Agenda

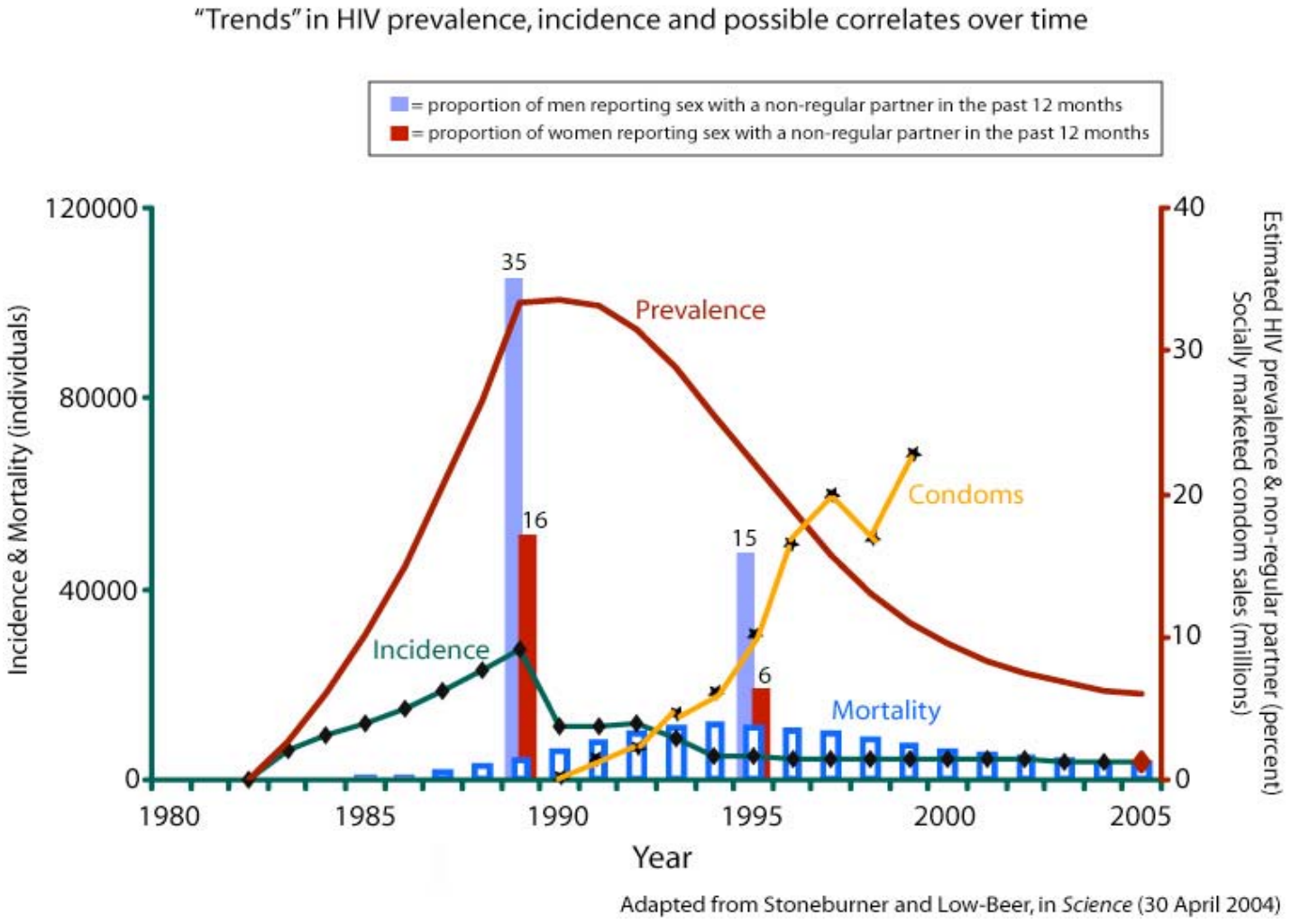
- Prevention is essential
  - Each year brings an estimated 5 million new HIV infections…
  - …and 3 million AIDS-related deaths
- A brief history…
  - early successes…followed by some more recent disappointments
- A strategic approach: identifying different priorities in different epidemic contexts
- Some key challenges and emerging opportunities
- Implications for programming
- Policy issues

Early successes: Thailand and “100% condoms”



Adapted from Stoneburner and Low-Beer: “Epidemiological elements associated with HIV declines and behavior change in Uganda: Yet another look at the evidence”

Early successes: Uganda and “zero grazing”



Adapted from Stoneburner and Low-Beer, in *Science* (30 April 2004)

Teenage pregnancy in Uganda

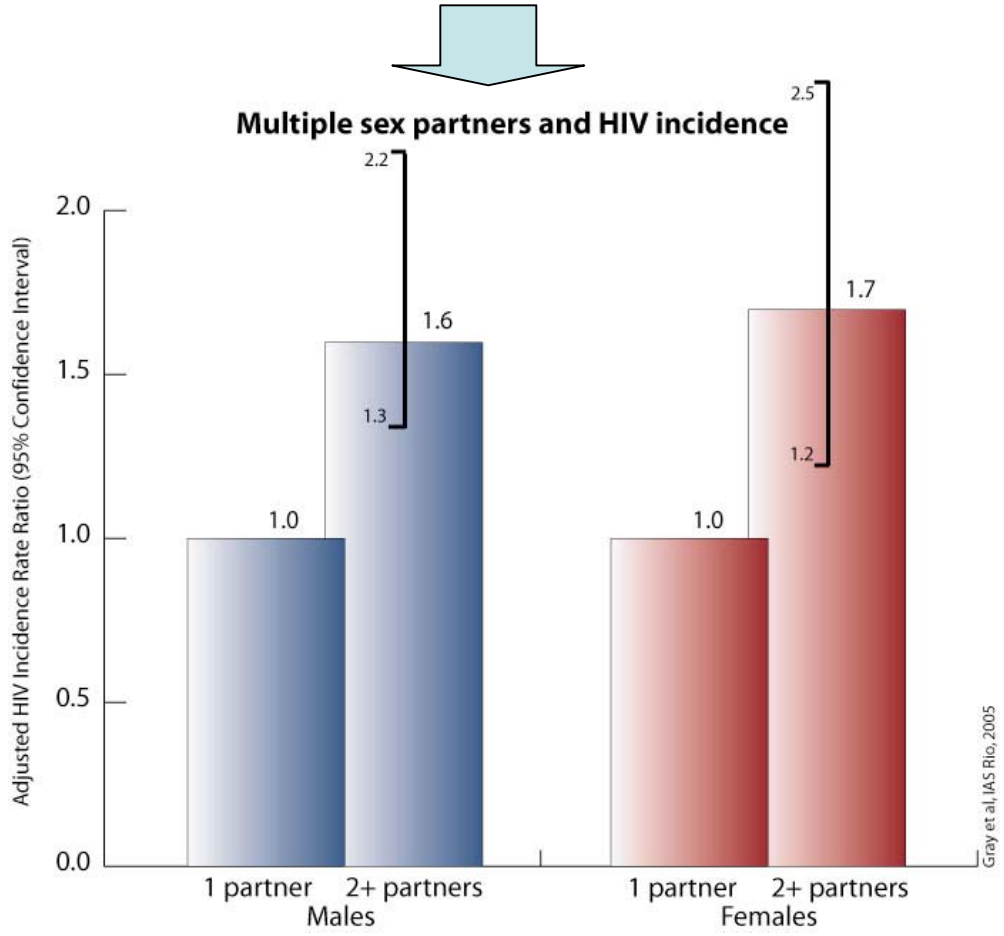
Percentage who have had children or who are currently pregnant

From Demographic and Health Surveys

	15 year olds	16 year olds	17year olds	18 year olds	19 year olds
1988	8.7	20.8	44.1	58.3	59.4
1995	7.7	22.1	43.3	64.7	70.8
2000/1	3.3	12.9	23.2	54.0	61.2

Multiple sexual partnerships

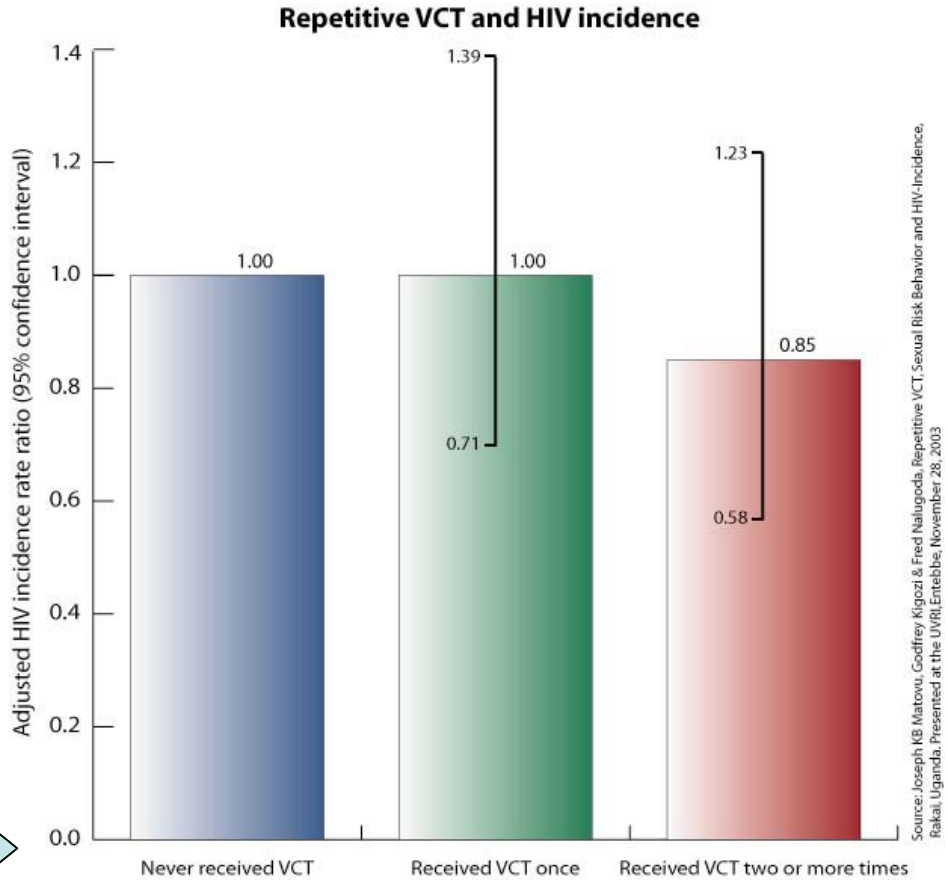
Worldwide, almost all studies show increased risks with increased sexual partners



*Partner reduction has been associated with declines in HIV at the population level in both **concentrated** and **generalized** epidemic settings*

HIV Counseling and Testing[1]

- HIV Counseling and testing (HIV CT) is an essential gateway to prevention, care and treatment services
- HIV CT may help prevent HIV transmission in discordant couples and from HIV+ individuals
  - Preventing partner violence and other adverse outcomes remains a priority[2]
  - 13 percent of acquiring partners in a Zambia discordant couple study were infected by via exposure *outside* of the primary partnership[3]
- However, the prevention benefits for HIV- individuals remain unclear…

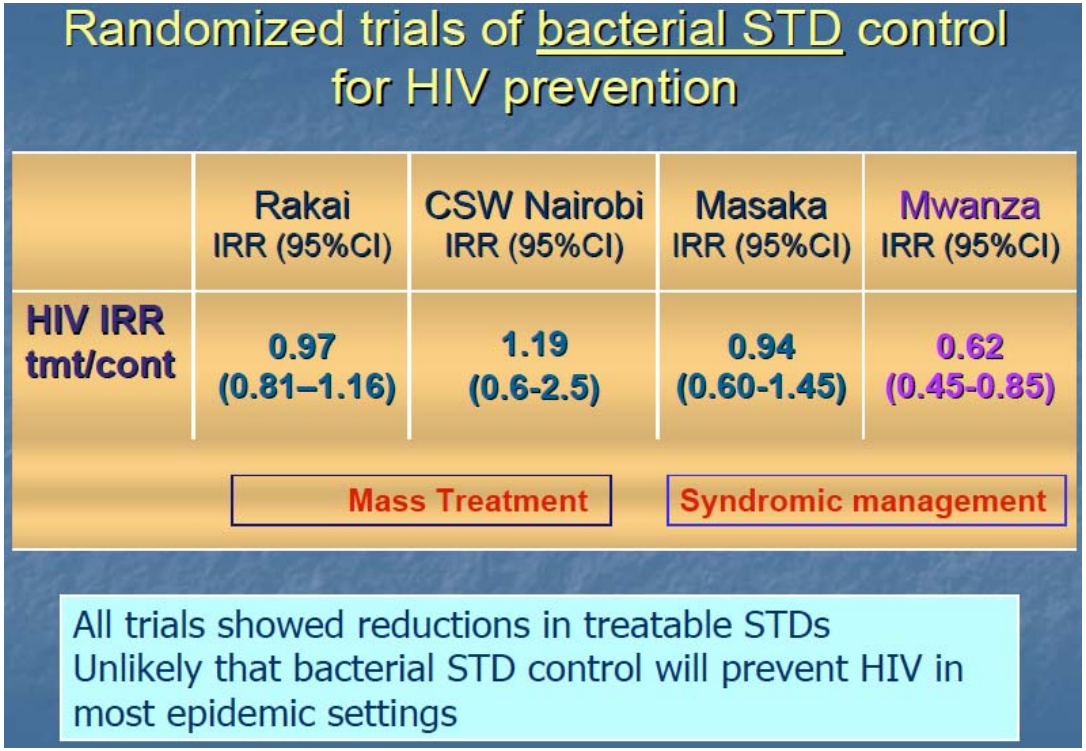


Promotion of prevention must be far more than just the promotion of HIV CT

[1]Weinhardt et al (1999); VCT Study Group, (2000); Allen, S, et al (2003); Matovu, KB, et al (2005); [2]Maman et al (2003); [3]Allen, S, et al, (2003)

STI Treatment[1]

- Observational data demonstrate a ***strong association*** between HIV infection and other STI infection
- ***But***, most of the randomized, controlled trials of STI treatment found no reduction in HIV infections



Gray et al, IAS Rio, July 2005

We're currently anticipating findings from HSV-2 suppression trials (HSV-2 seems likely to increase both HIV acquisition and infectivity)

[1]Grosskurth et al (2000);Kamali et al (2003); Kaul et al (2004)

Nonoxynol-9[1]

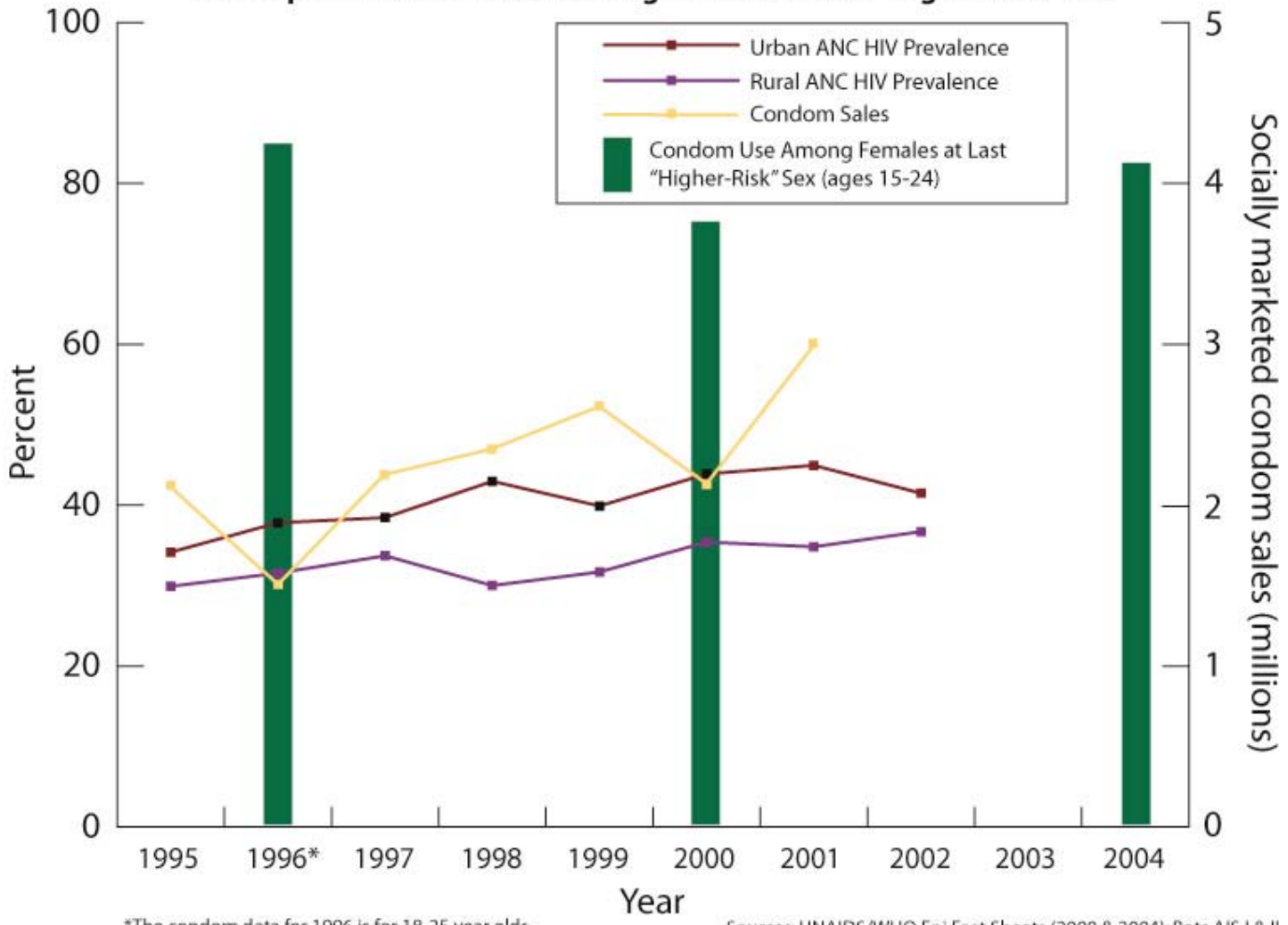
- Great hopes for a female-controlled method
- But, one study found that HIV infection risk among frequent users was nearly twice that of placebo users

General population condom promotion[2]

- Remarkable “successes” in general population condom promotion don’t seem to have been accompanied by declines in HIV prevalence in generalized epidemics…

[1]Van Damme, et al (2002); [2]Hearst and Chen (2004)

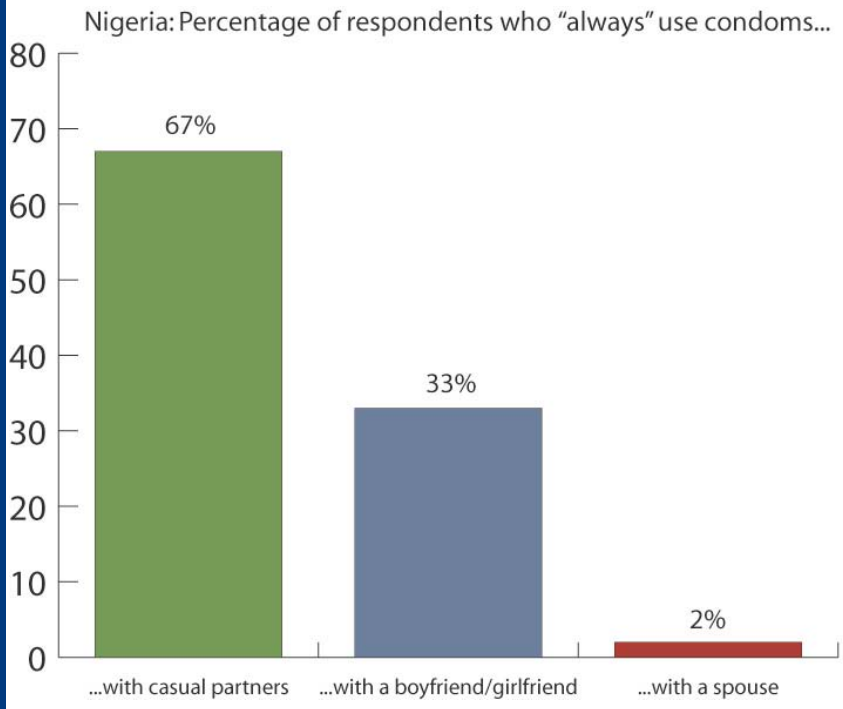
Botswana: "Trends" in HIV Prevalence at ANC Surveillance Sites and Reported Condom Use Among Females at Last "Higher-Risk" Sex

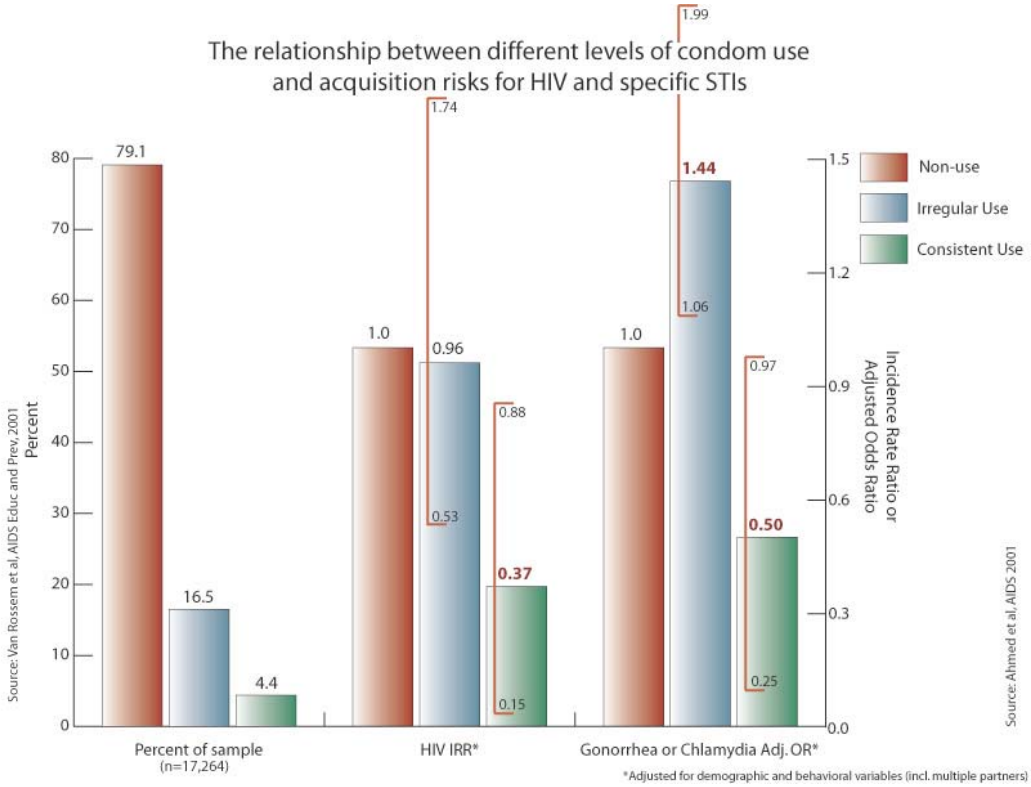


*The condom data for 1996 is for 18-25 year olds

Sources: UNAIDS/WHO Epi Fact Sheets (2000 & 2004); Bots AIS I & II

Condoms can dramatically reduce HIV infection risk (by about 85%)…when they are used *correctly* and *consistently*…





…however, programming to achieve consistent use in the general population has been a challenge…and *inconsistent use* seems to afford *little to no protection*…

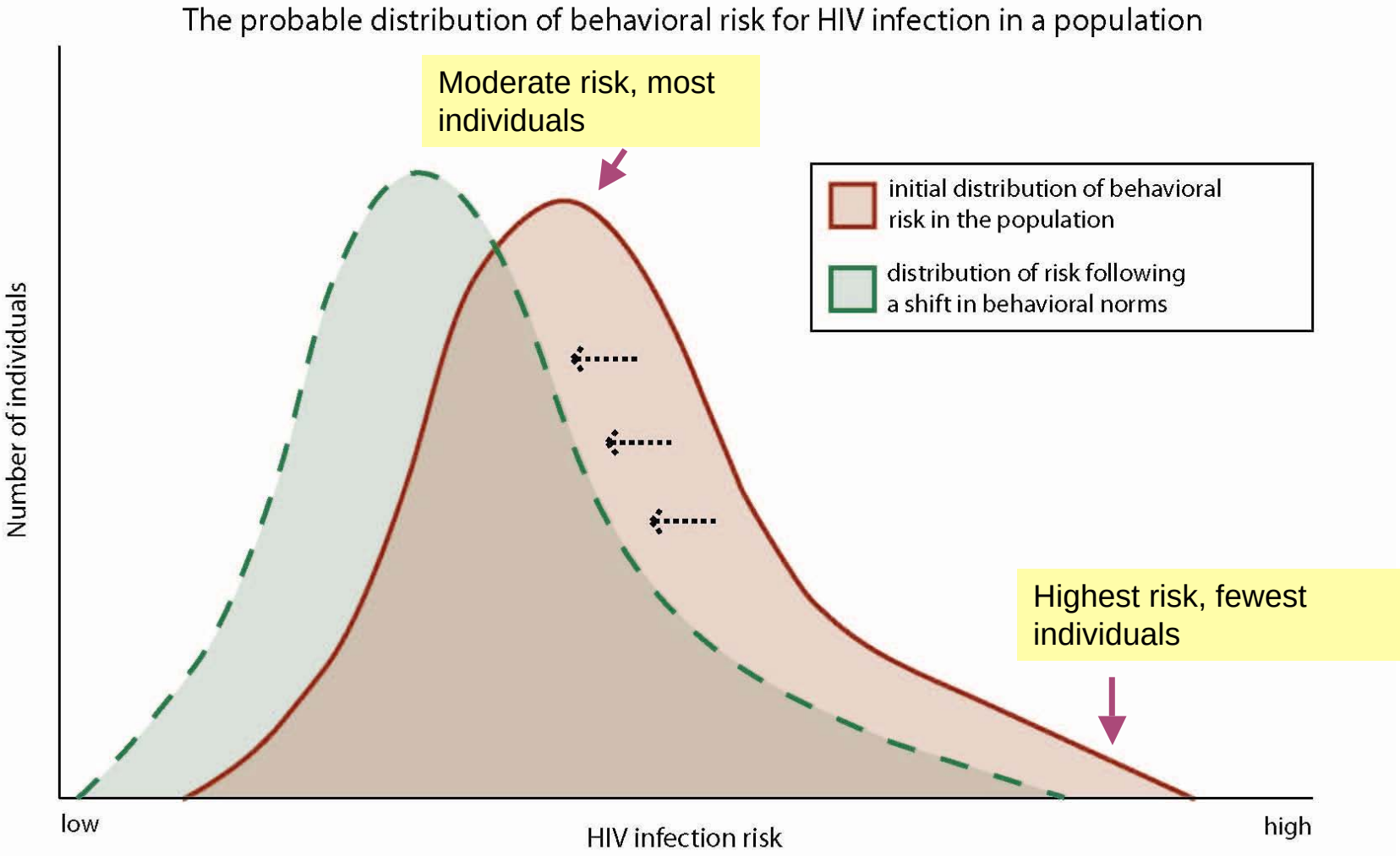
Predicting the spread of infectious diseases:

$$R_0 = \beta D C$$

- R_0 — *Secondary spread of disease agent*
- β — *Transmission efficiency*
- D — *Duration of infectiousness*
- C — *Number of individuals exposed*

Source: May RM, and Anderson, RM Transmision Dynamics of HIV infection. *Nature* 326, 137-142 (1987)

Using evidence to set strategic priorities



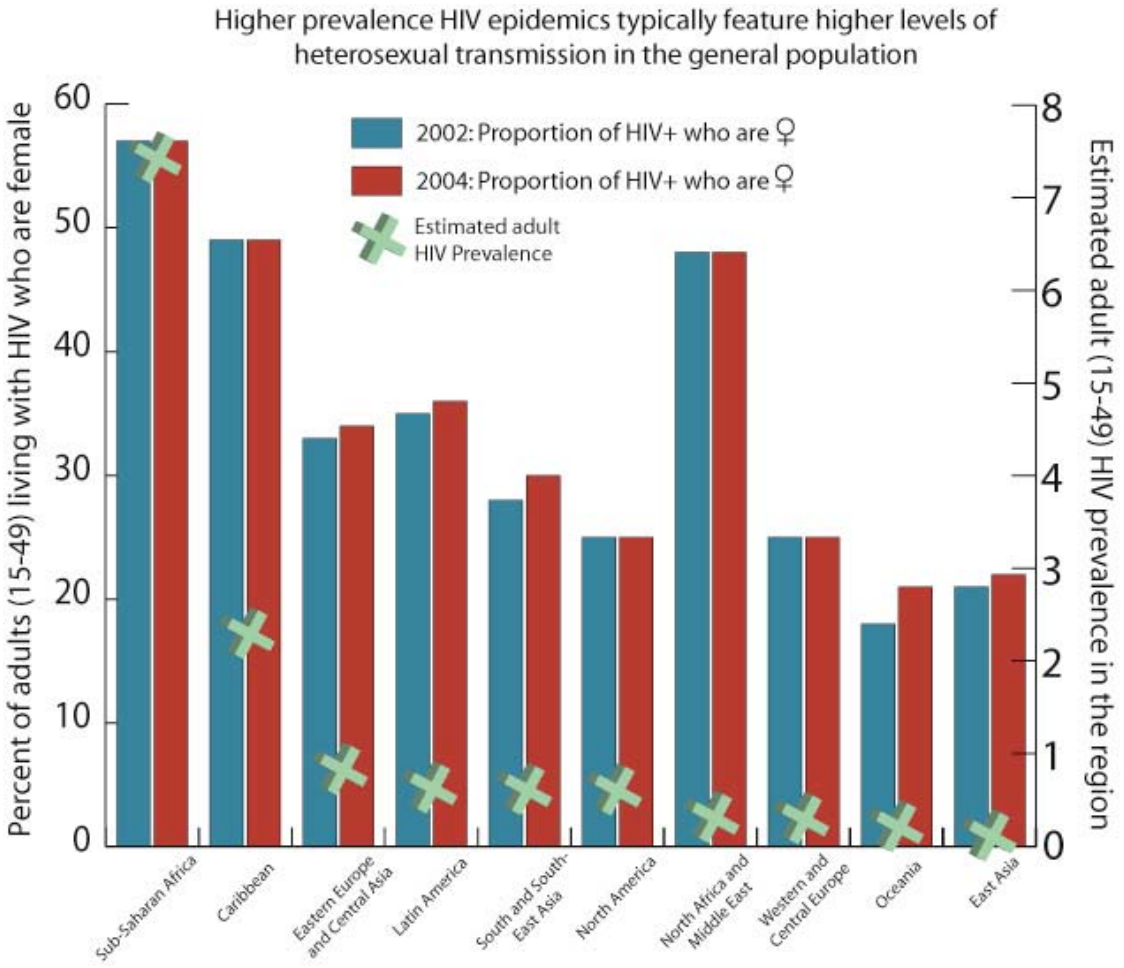
Adapted from Rose G, The Strategy of Preventive Medicine, 1992

Concentrated vs Generalized epidemics

Concentrated: Most new infections can be attributed to higher-risk contexts (i.e.: MSM, IDU, CSW, etc…)

Generalized: Most new infections come from heterosexual contact in the general population

Concentrated vs Generalized epidemics

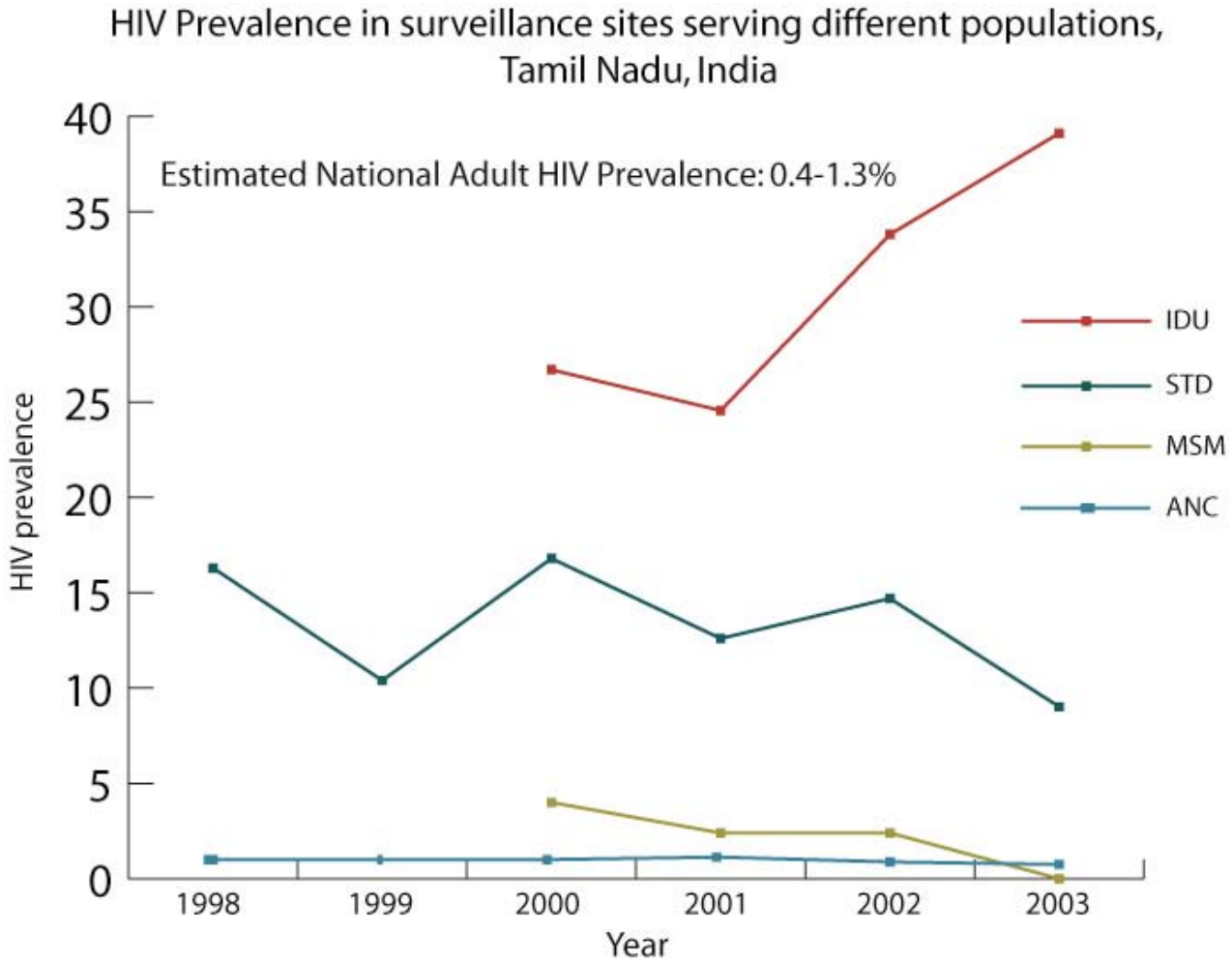


Source: UNAIDS AIDS Epidemic Update 2004

In concentrated epidemics, one may see an increasing proportion of new infections among girls and women through "bridging" from higher-risk partners…

…however, concentrated epidemics are unlikely to "evolve" into generalized epidemics, because they are fueled by ***different sources*** *of new infections…*

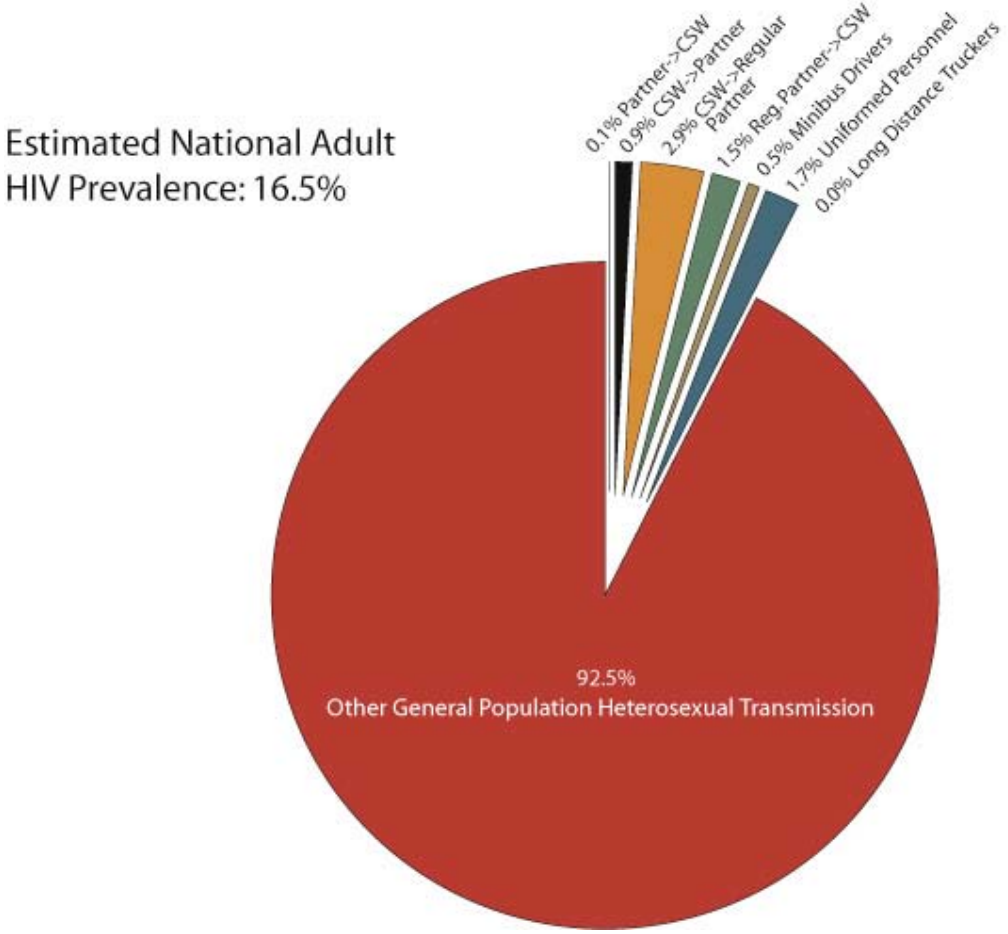
India's concentrated epidemic



Source: National AIDS Control Organization, GOI, accessed online @ http://www.nacoonline.org/facts_overview.htm

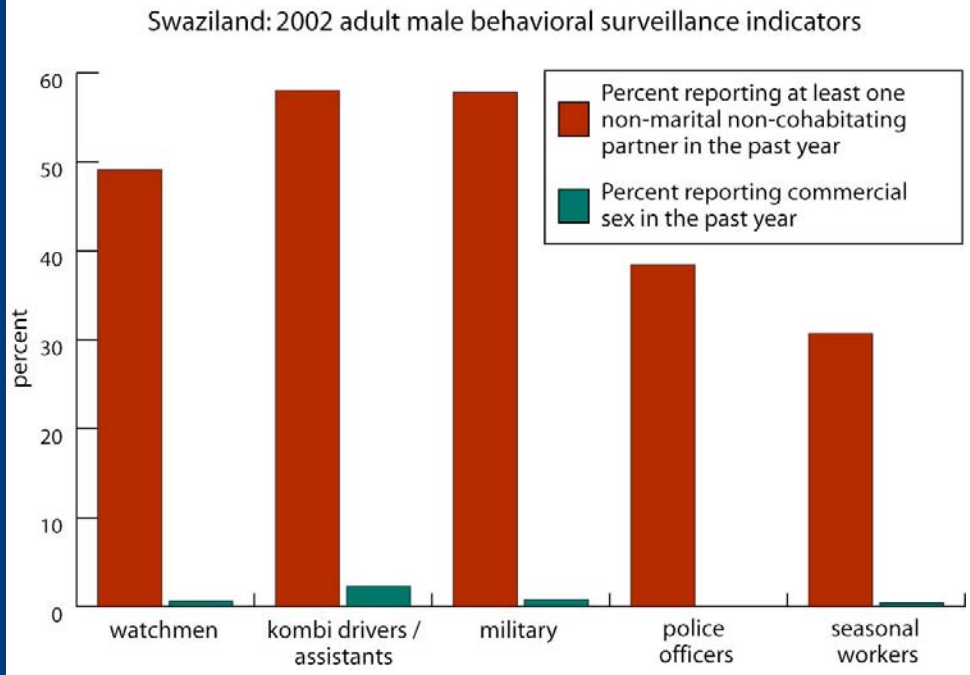
Zambia's generalized epidemic

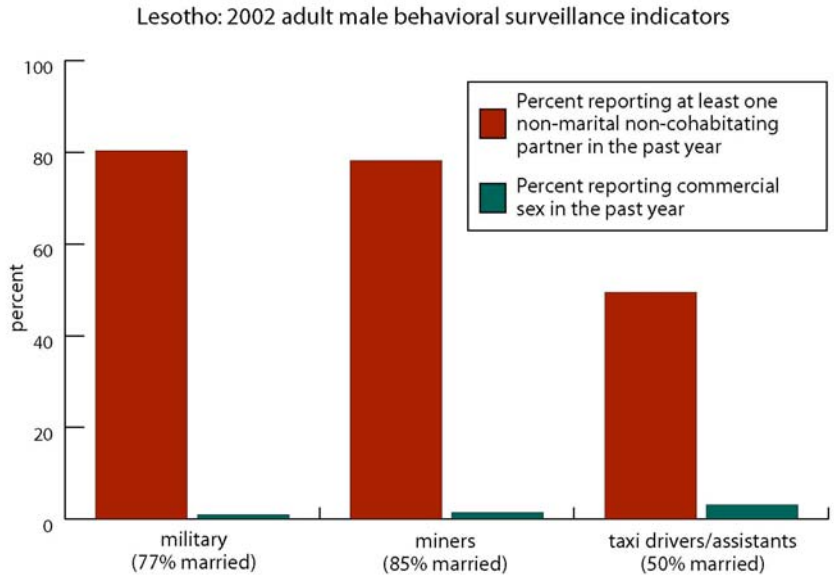
Zambia: Relative Proportion of Incident Cases (modeled)



Source: personal communication, Mark Shields (Zambia)

Low levels of “highest-risk” sex in high-prevalence epidemics

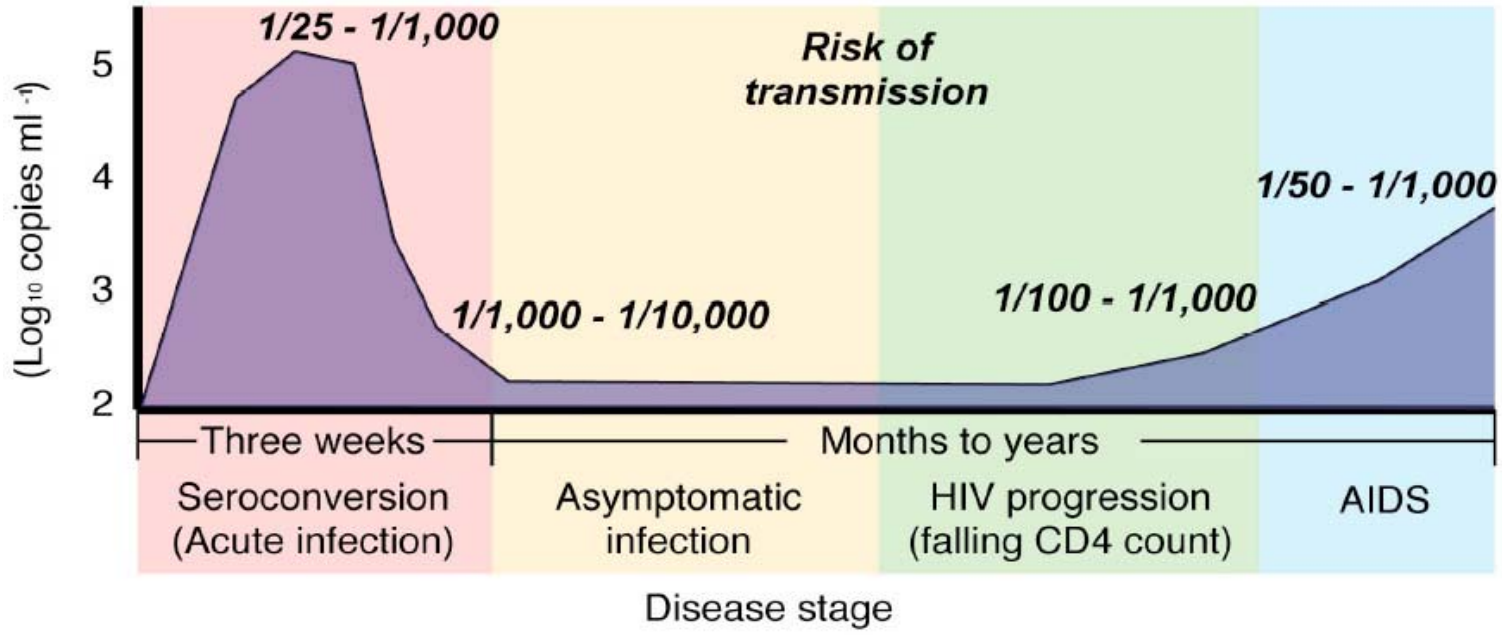




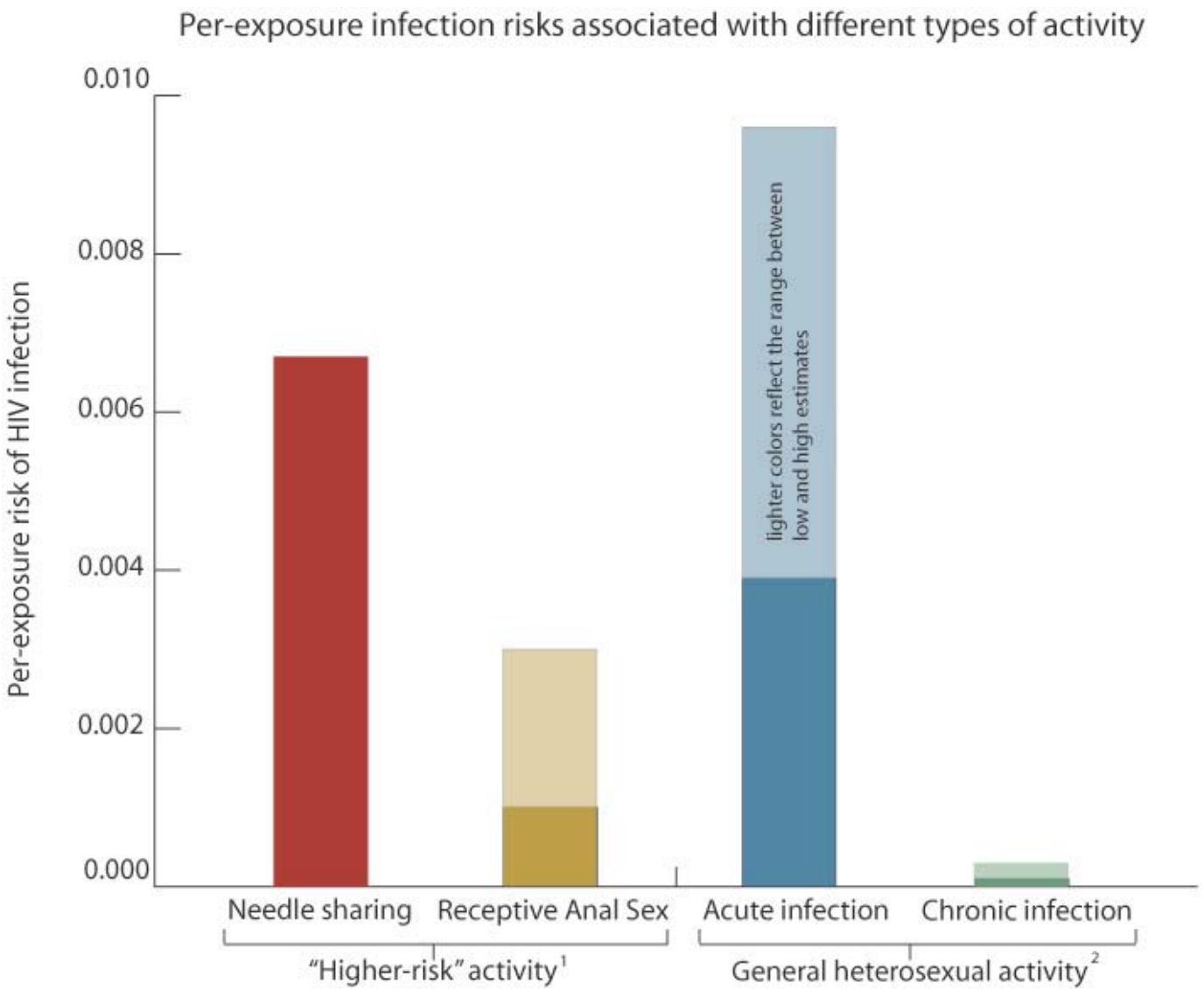
Transmission efficiency

"Mathematical models estimate the average probability of male–female transmission of HIV-1 per unprotected coital act to be between 0.0005 and 0.003% during chronic HIV infection, ***which in itself would not sustain an epidemic****."*

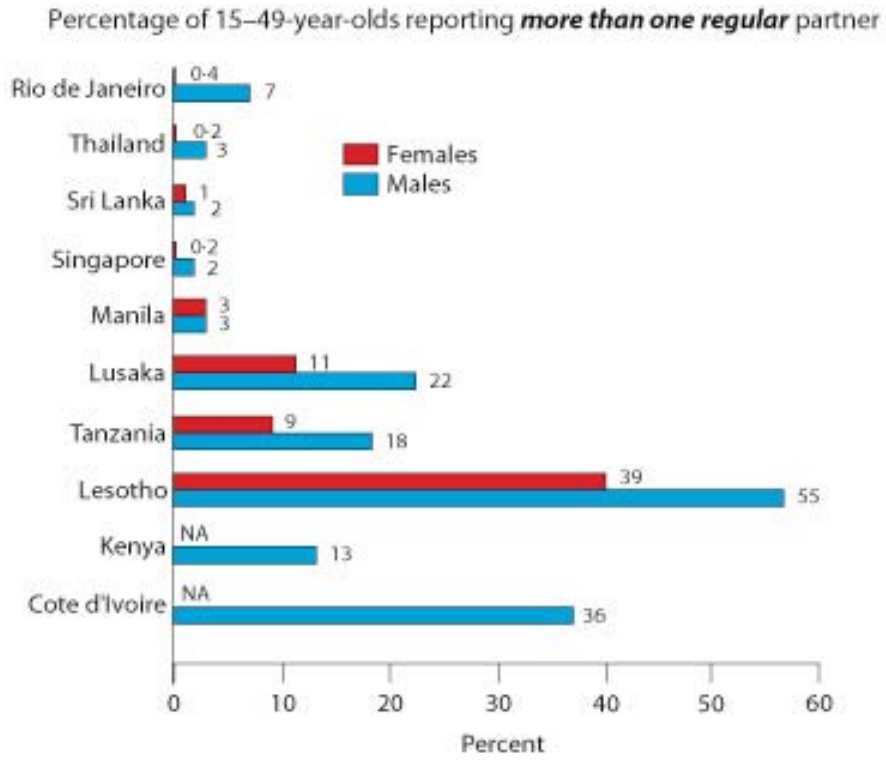
-Pao et al, AIDS (2005)



Source: Galvin, S.R. & Cohen, M.S. (2004) The role of sexually transmitted diseases in HIV infection. Nature Reviews Microbiology, 2(1).


Per-exposure infection risks associated with different types of activity
Per-exposure risk of HIV infection
0.010
0.008
0.006
0.004
0.002
0.000
lighter colors reflect the range between low and high estimates
Needle sharing
Receptive Anal Sex
Acute infection
Chronic infection
"Higher-risk" activity[1]
General heterosexual activity[2]
1Medical Management of HIV Infection, 2004 Edition, Bartlett and Gallant (eds.);
2Chakraborty et al(2001)AIDS, 15(5)

Concurrent partnerships



Caraël M. Sexual behaviour. In: Cleland JG, Ferry B, eds. Sexual behaviour and AIDS in the developing world. London: Taylor and Francis, 1995.

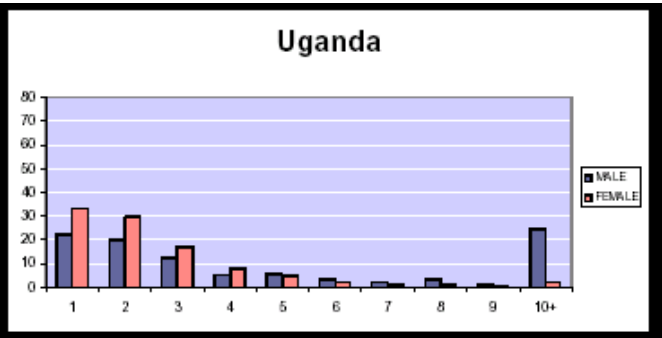
*Acute infection may make the **timing** of sexual partnerships more important than the **number** of partnerships with respect to HIV transmission*

Uganda

18% HIV+

1994

(*Rakai Sexnet* study)

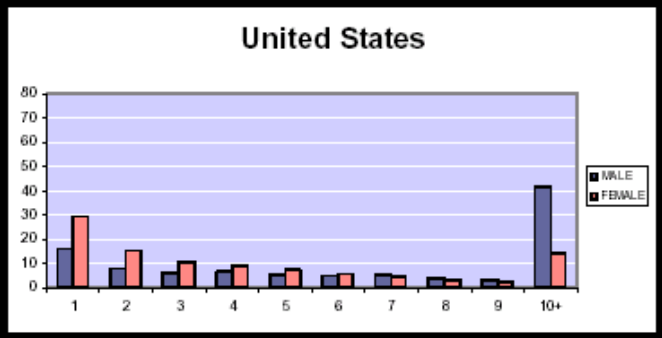


United States

1% HIV+

1994

(*NHSLS* study)

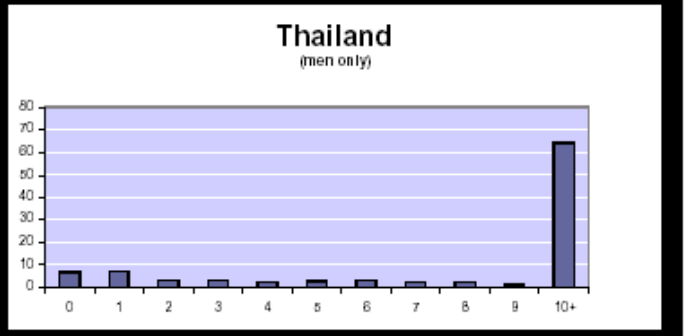


Thailand

2% HIV+

1993

(*BRAIDS* study)



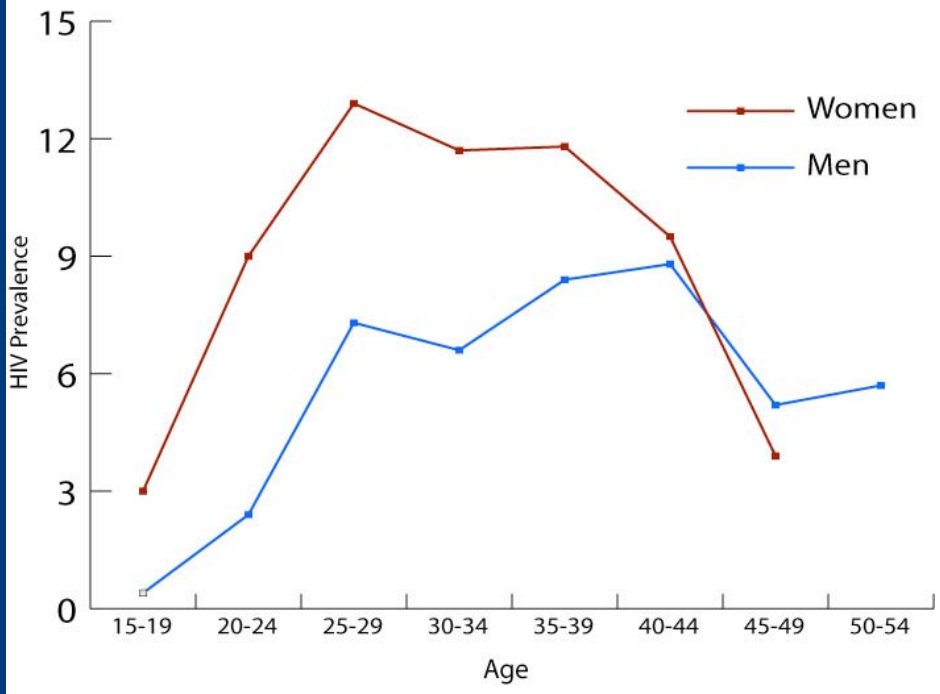
UW Network Modeling Project
Martina Morris, PI

NIH Council June 2003

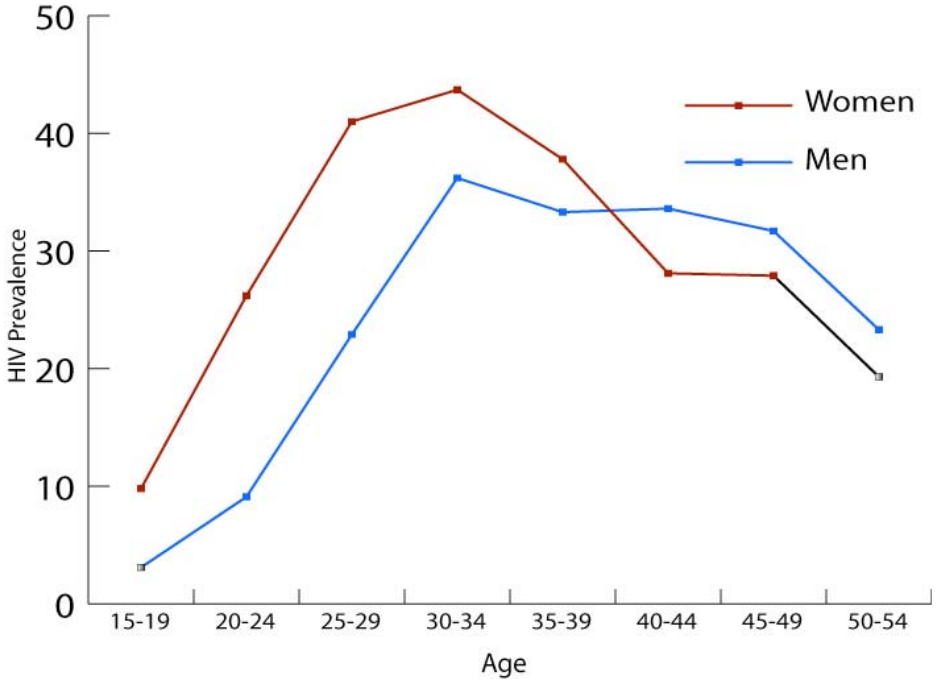
Cross-generational sex

Although studies* suggest that women are not biologically more susceptible to HIV infection than men, the vulnerability of girls and young women is a key concern…

HIV Prevalence by Age and Gender: Kenya 2003 DHS



HIV Prevalence by Age and Gender: Botswana 2004 BAIS



Older men make riskier partners than young men…
…it may be essential to address adult male behavior to reduce the HIV risks faced by young women

*See in particular Gray et al in Lancet 357: 1149-1153, 2001

Sexual coercion among females, Rakai, Uganda

- Coercive first sex 14.4%
- Coercive sex 15-19 20.6%
- Coercive sex 20-24 31.1%
- All women 34.2%
- Increased coercion risk in:
  - Younger women <15 OR=1.6
  - Earlier age at first sex OR=1.5
  - Alcohol* use by male OR=2.8
  - Perception of HIV risk OR=2.9

Source: Koenig *Soc Sci Med* 2004, Zablotska 2004

**Alcohol may also prove an important focal point for prevention efforts, as it may increase both biological and behavioral risk for HIV infection*[1]

[1]Talbot, EA, et al, Int J STD AIDS 13(5),2002; CDC AIDS Surv Rept. 13(1), 2001; Bagby, G et al, Alcoholism: Clinical and Exp. Res., 2003

Emerging innovations

- **Microbicides[1]:**
  - Models assume that may reduce per-act transmission risk by 50 percent
  - Must apply before each sex act
- **Pre-Exposure Prophylaxis (PREP)[2]:**
  - A pill-a-day for prevention
  - RCTs currently underway in SF, Nigeria, Cameroon*, Ghana, Botswana, and Thailand
  - No current efficacy estimates
- **Vaccines[3]:**
  - Wide estimates of possible risk reduction, in the range of 25 to 75 percent
  - Current candidate vaccines will require multiple doses.
- **Male circumcision[4]:**
  - One-time procedure to confer prevention benefits
  - RCTs currently underway to explore actual risks and benefits

[1]Dilley et al (2003); Dukers et al (2001); Stolte et al (2004); Tun et al (2003); Gremy et al (2004)

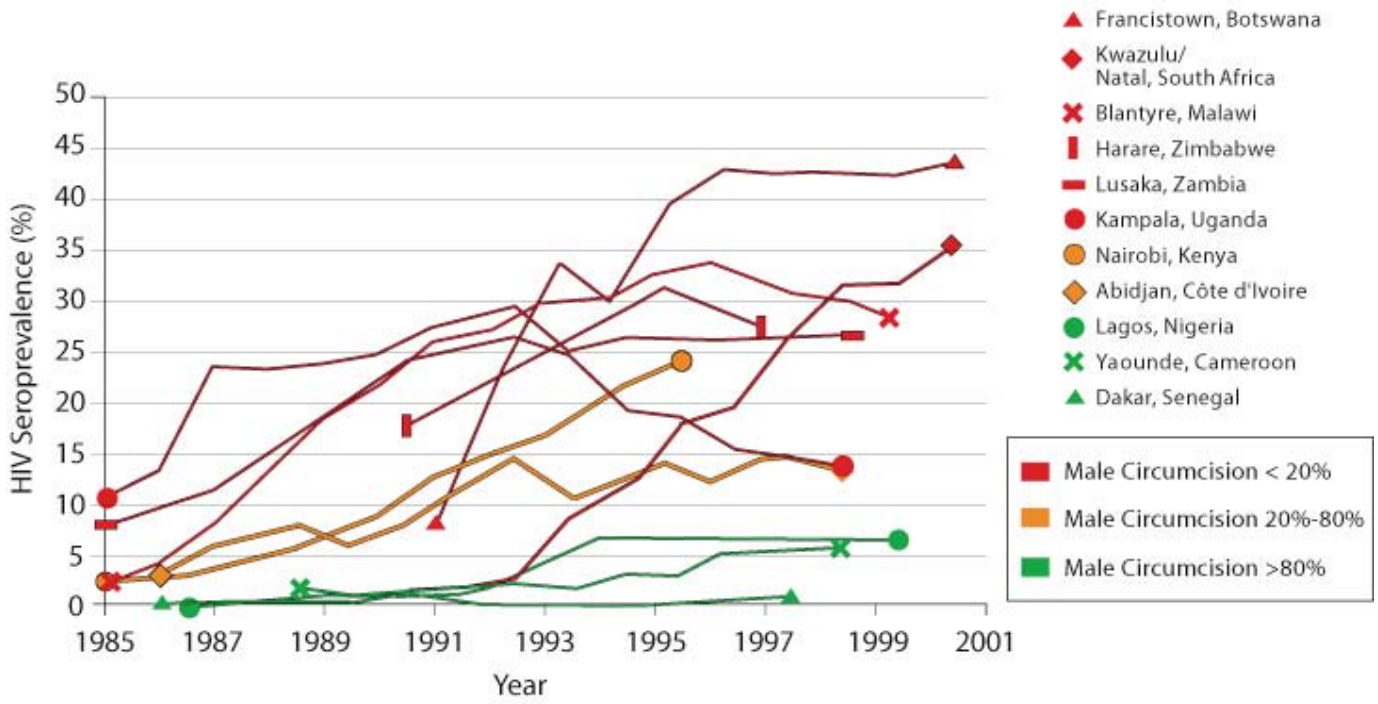
[2]Bruckner and Bearman, Journ of Adol Health, 36, (2005)

[3]Gray et al, (2003)

[4]Weiss et al (2000); Reynolds et al (2004)

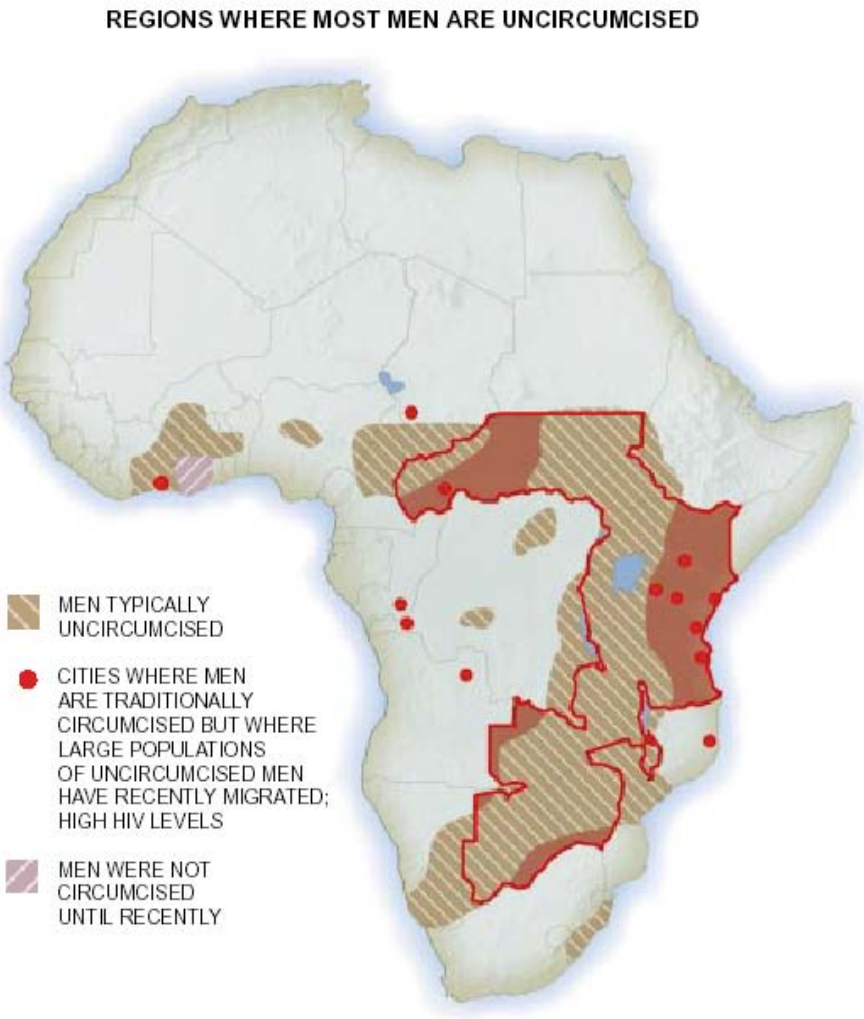
Male circumcision

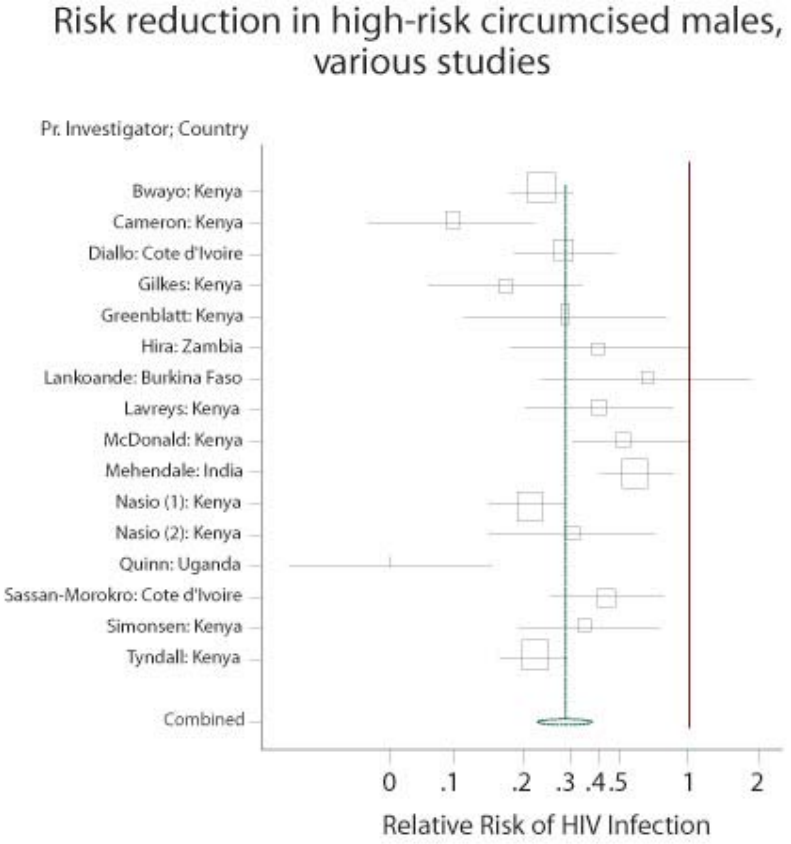
HIV seroprevalence for pregnant women, 1985 - 2000,
and estimated male circumcision rates, selected urban areas of Africa



Adaptation of D. Wilson slide. Source: U.S. Census Bureau HIV/AIDS Surveillance Data Base 2000; Halperin DT, Bailey RC. Male circumcision and HIV infection: 10 years and counting. Lancet 1999 354;9192:1813-5.

Male circumcision





Notes 1) Relative risk of .2 means that circumcised men are 1/5 as likely as uncircumcised men to acquire HIV infection; relative risk of .5 means 1/2 as likely; etc.

2) Horizontal lines represent confidence intervals; rectangles indicate relative size of study populations.

H. Weiss et al. Meta-Analysis. USAID Male Circumcision Meeting, Sept. 2002.

Male circumcision

Unadjusted RR

RR_0 : 0.35 (0.20-0.60) Protection : **65%** (40-80)

Adjusted RR

(age, religion, ethnic group, alcohol consumption, recruitment period)

RR_1 : 0.33 (0.19-0.57) Protection : 67% (43-81)

Adjusted RR

(…, marital status, condom use, # of sexual partners, # of sexual contacts)

RR_2 : 0.34 (0.20-0.59) Protection : 66% (41-81)

Per protocol unadjusted RR (no dilution effect due to cross-over)

RR_3 : 0.25 (0.14-0.46) Protection: 75% (64-86)

All p < 0.0002

Bertran Auvert – IAS 2005 – 27 July- Orange Farm intervention Trial (ANRS 1265)

Risk compensation

An example: seatbelts and motor vehicle injuries[1]:

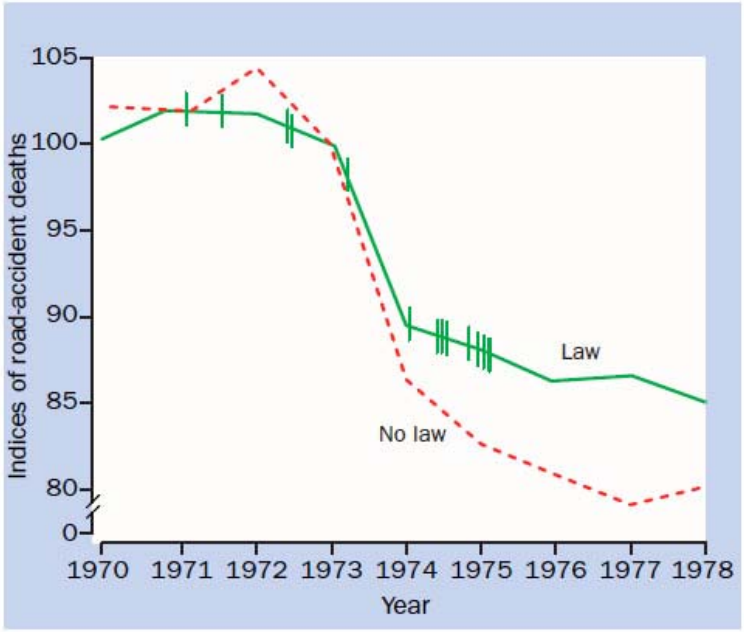


Figure 1: **Indices of road-accident deaths for 13 countries with and four countries without seat-belt laws**

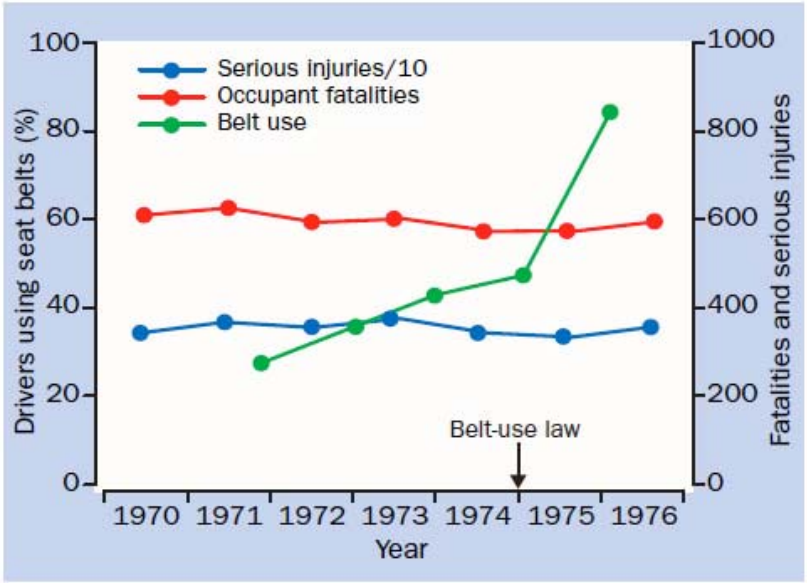


Figure 2: **Motor-vehicle-occupant fatalities, serious injuries, and seat-belt wearing, Sweden**

A number of studies have found that the mere promise of expanded access to ARV treatment or to post-exposure ARV prophylaxis has been associated with ***significant increases in risky behavior[2]***

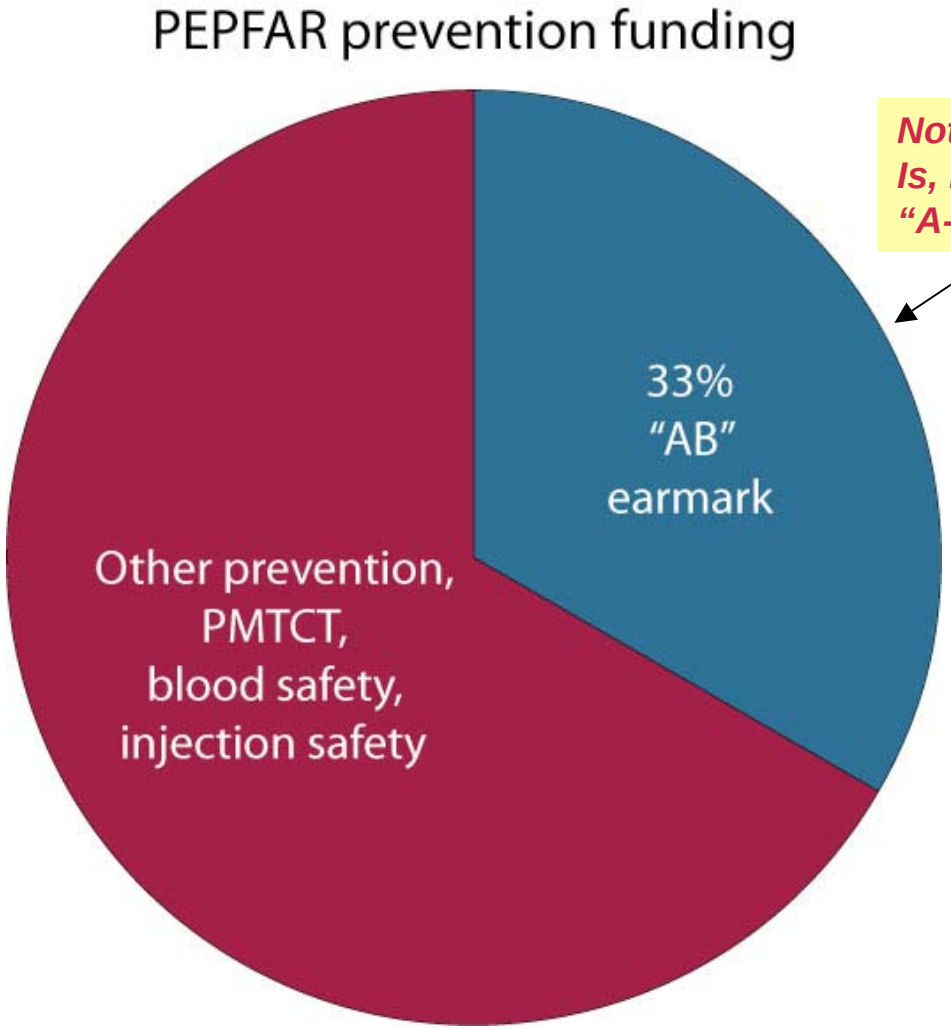
[1]Richens J, et al (2000)

[2]Dilley et al (2003); Dukers et al (2001); Stolte et al (2004); Tun et al (2003); Gremy et al (2004)

Setting clear priorities

- ***Generalized epidemics:***
  - *Most transmission through heterosexual sex in the general population*
  - ***Lead with the "B":*** *Partner reduction as a key priority*
  - *Work to* ***mobilize social capital*** *and* ***change social norms*** *and shift the risk distribution curve*
  - *Balance the emphasis on ABCs as epidemiologically appropriate*
  - *Strategize to achieve population-level benefits, tailor programs to address individual-level needs*
  - *Take a proactive stance towards minimizing risk compensation and maximizing the potential benefits of prevention "innovations"*
- ***Concentrated epidemics:***
  - ***Maintain focus*** *on condom promotion and other forms of risk reduction for high-risk contexts*

Prevention policy and earmarks



Note that the earmark Is, in fact "AB" and <u>not</u> "A-only"

Condom Programming with PEPFAR funds

- *Funds may be used in schools to support school-based programs that deliver age-appropriate ABC information for young people above age 14*
- *Funds may be used to support integrated ABC programs that include condom provision in out-of-school programs for youth identified as engaging in, or at high risk for engaging in, risky sexual behaviors*
- *Funds may **not** be used to physically distribute or provide condoms in school settings*
- *Funds may **not** be used in schools for marketing efforts to promote condoms to youth*
- *Funds may **not** be used in any setting for marketing campaigns that target youth and encourage condom use as the primary intervention for HIV prevention*

STI Programming with PEPFAR funds

- *STI Dx and Rx can be supported for populations at increased risk and PLWHA*
- *HIV counseling and testing can be supported (and is encouraged) in STD clinical settings*
- *STI drugs and reagents can be supported as part and parcel of improved services for most-at-risk groups and PLWHA*
- *STI Dx and Rx are not supported in primary care and family planning settings (low risk)*
- *General population syndromic validation studies and training are not supported*

Prostitution and Sex Trafficking

- The US Leadership Against HIV/TB and Malaria Act of 2003 mandates that: "*no funds made available to carry out this Act...may be used to promote or advocate the legalization or practice of prostitution or sex trafficking.*"

However:

- It goes on to say…"*nothing in the preceding sentence shall be construed to preclude the provision to individuals of palliative care, treatment, or post-exposure prophylaxis, and necessary pharmaceuticals and commodities, including test kits, condoms, and when proven effective, microbicides.*"

<u>Nothing</u> in PEPFAR prohibits the USG or any of our partners from providing services to women in prostitution.

Many thanks!